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Eosinophilic Esophagitis: Practical Aspect of Immediate and Delayed Hypersensitivity Food Testing

Background

Eosinophilic esophagitis is a recently recognized disorder consisting of a recognizable pattern of symptoms and abnormal esophageal histology. Food allergy has been recognized as a factor in eosinophilic esophagitis. This handout is intended to provide a template for approaching immediate hypersensitivity skin testing and delayed hypersensitivity skin or patch testing in patients with eosinophilic esophagitis.

Immediate Hypersensitivity Testing

Skin Test Technique

It is recommended that skin testing be done with an individual prick/lancet devise rather than a multitest device. This allows better spacing between tests and allows testing with fresh foods. If using commercial foods the skin testing is done by the traditional prick test technique. When using fresh or native foods the skin test device can be dipped in a liquid food such as milk or egg white and then the skin is pricked. When testing for fresh foods that are in the form of a paste it is sometimes helpful to place a small amount of the food on the skin and then prick through the food. See Appendix B for fresh/native food preparation. It is recommended that the back is used for skin testing. This will allow appropriate spacing between tests. Patch testing cannot be done on the same day as prick skin testing.

Recording of skin tests should be done by **measuring wheal over flare size.** This will allow easy comparison with future testing or sharing information with other allergists.

Selecting Allergens

There is no standard panel of foods for testing in eosinophilic esophagitis. The selection of foods should consist of a basic panel of foods and then additional foods added based on the patient's diet. In individuals with ethnic diets (eg.lentils) you may need to test the food after preparation by the family. See Appendix A for a suggested list of foods.

Food allergens for testing are readily available through commercial extract companies. However there is no standardization of food allergens. The use of fresh foods allows the physician to be assured that the foods chosen for testing are always valid. Previous studies (Holbreich M. JACI 121,2.pS251) have shown greater sensitivity with fresh foods then with commercial foods.

Test Interpretation

The test is considered positive when the wheal size is 3 mm greater than control and with an associated flare. This indicates the presence of IgE mediated sensitivity but does not necessarily correlate with induction of esophageal inflammation upon ingestion. **Test results may change over time and repeat testing in 18-24 months can be helpful.**

Delayed Hypersensitivity Skin Testing for Foods in Eosinophilic Esophagitis

Background

Easily identifying the foods associated with eosinophilic esophagitis is difficult. Therefore using delayed hypersensitivity testing or patch testing has been recommended for the identification of foods which may play a role in eosinophilic esophagitis. As with skin prick testing the correlation between the presence of a positive patch test to a food, food elimination and significant improvement in eosinophilic esophagitis is difficult to establish. What follows is a template for the use of patch testing in eosinophilic esophagitis.

Food Selection for Patch Testing

The same selections of foods that are used for skin prick testing are often used for patch testing. It is up to the physician to determine whether or not they want to patch test for foods that are positive on skin testing. Seeds and nuts other than peanut are generally not used in patch testing (personal recommendation). Caution should be used in selecting foods that may cause a significant local irritation under the patch such as spices.

Patch Testing Technique

Patch testing is done by applying a Finn chamber (SmartPractice formerly Allerderm Laboratories: www.finnchamber.com) filled with an individual food and applied to the back. When possible 12 mm chambers should be used for all foods and a 12 mm chamber is always used for milk. In smaller children their back may be too small to apply individual 12 mm chambers and it is better to use the 8mm Finn chambers that are available as 10 tests per patch strip. See Appendix B for food sources and preparation.

Application of Patch Test

1. Place the individual Finn chambers on a Mayo stand or similar flat surface.

2. Using a number key for each food, write the corresponding number on each individual patch test (non stick side or the side showing once applied). Peal the paper from the patch to reveal the well leaving the small strip of paper on the edge. When using the 12 mm chambers it is a good idea to write the test number on the small paper strip that will remain until removed just before application. This will assure no mistakes in filling chambers.

3. Fill the Finn chamber with the appropriate food prepared in accordance with the recommendations in appendix B. Do not overfill the Finn chamber wells. Fill the chambers just before testing as foods dry out quickly.

4. Have the patient remove their shirt exposing the back. Locate an area on the back where there is ample flat space to apply the patches. Avoid areas around the scapula where movement may disturb the patches. The lower back often provides the flattest area. Clean off the selected area with alcohol. Have the patient stand with their shoulders slightly back as if they were carrying a backpack. For younger children and
infants have them sit on the parent's lap with their faces toward the parent. Carefully remove the paper from the unexposed covered edge of the patch and place the patch on the back. Hold the patch very taught and apply to the back avoiding wrinkling of the patch. Apply the lower edge of the patch to the back and move up towards the top of the patch for smooth application. One chamber should be a control patch with no food in the chamber.

5. After the wells have been sealed to the back use a black Sharpie marker and write the corresponding number from the patch on the skin adjacent to the patch.

6. Draw a basic map on a recording sheet locating the presence of each patch by number. This will allow identification if numbering fades after the patches have been removed.

7. If the patches appear to be lifting off the skin or if they lift off the skin during the 48 hours of application medical tape (Cover-Roll Stretch:BSN-JOBST 6 in x 10 yards) can be placed over the patches. The patches generally stick well and the use of supplemental medical tape is not frequently required. We supply enough tape for application if necessary.

8. Provide the patient or parent was written instructions concerning care of the patch test area during the 48 hours of application. See patch test instructions.

Removal of the Patches

After 48 hours the patches are removed from the back by a family member. Food residue can be gently removed with a washcloth being careful not to remove any of the numbers needed for reading.

Reading the Patch Test

Patch test results are read at 72 hours after application and 24 hours after removal. Reading is done by the allergist. Interpretation of patch test results is difficult and there may be areas with minimal amounts of irritation, areas with inflammation only and areas with obvious reactions. After doing a number of patch tests the physician will get a sense of test interpretation. In general the following scale is used:

0: No reaction
+1: Single or scattered red papules with minimal induration and erythema
+2. Macular erythema with minimal induration
+3: Significant erythema with vesicles
+4: Significant induration with erythema or significant vesicles with erythema

Patch Testing: Patient Instructions

1. Do not shower, bathe or wash the patch test site.
2. Do not apply creams, lotions or soaps to the patch test area
3. Do not scratch or rub the patches
4. The wells need to stay in direct contact with this skin for 48 hours. If the patches are lifting off apply medical tape to keep the wells attached to the skin.
5. It is normal to have some itching during the test period. Benadryl may be used to relieve itching.
6. After 48 hours from the time of the patch test application, gently remove patches and wash off the back with water. Leave the "sharpie" numbers on the skin to aid in patch test reading. No showers or baths are permitted until the final reading has been completed. Please mark below any sites that are red or inflamed at 48 hours.
7. The patch test results are read by the physician 72 hours from the initial application.
8. Call our office for questions that may come up during the test period. Call if there is significant pain at the test site.

REMOVAL_____

48 Hour reading: list number of any patch test sites that are "red"

Supplies for patch testing

- 3 cc BD oral dispensing syringes with caps: available in bags of 100
- stir straws
- paper towels
- sterile water
- triple beam balance or digital scale (Ohaus Scales)
- patch tests (finnchamber.com) purchase both 12 mm individual patches and 10 8mm wells per patch if testing young children
- Sharpie marker
- medicine cups
- tongue depressors
- Mayo stand or similar movable work space to hold patches
- patient instruction forms
- recording forms
- appropriate foods

FOOD PATCH TEST

Name_____ **Date Applied_____**
DOB_____ **Date Read_____**
Referring Physician_____
Technician_____

Reading Grading:
0: No reaction
+1: Single or scattered red papules with minimal induration and erythema
+2. Macular erythema with minimal induration
+3: Significant erythema with vesicles
+4: Significant erythema with induration or erythema with significant vesicles

FOOD	GRADE	COMMENT
1. Milk		
2. Wheat		
3. Corn		
4. Beef		
5. Egg		
6. Potato		
7. Chicken		
8. Soy		
9. Barley		
10. Oat		
11. Rice		
12. Peanut		
13.Turkey		
14.Apple		
15.Peach		
16.Green bean		
17.Carrot		
18. Control		
19.		
20.		

Appendix A: Suggested Foods for Immediate Hypersensitivity Skin Testing

The following is a list of foods that had been recommended for skin testing. The final choice of the physician is based on the patient's history, age and diet.

Food Panel for Eosinophilic Esophagitis: Prick testing

Beef, chicken, egg, milk, corn, wheat, peanut, soybean, fish, turkey, barley, rice, oat, pork, tree nuts, mustard seed, green been, pea, carrot, white potato, sweet potato, apple and peach.

Food Source for Prick Testing

If the physician is doing both immediate and delayed hypersensitivity skin testing, some foods that have been prepared for patch testing are now readily available for prick testing. It is highly commended that allergists who are evaluating patients with eosinophilic esophagitis determined within their practice setting the results from using either commercial or fresh foods. Remember commercial food preparations are not standardized.

Personal Observations

I have found that using fresh milk and fresh egg is very reliable for prick skin testing. I do this for both routine testing for food allergies and in eosinophilic esophagitis. I have also observed that a number of grains particularly corn are best done with freshly prepared flours. Seeds, peanuts and tree nuts as well as fish appear to be perfectly adequate in commercial preparations for prick testing. Caution: some ALK walnut and pecan do not contain relevant protein. Caution must also be used in interpreting grain allergies and concomitant grass allergy. There may be cross reactivity.

I would strongly recommend that if you evaluate children and adults with immediate hypersensitivity skin testing that you give serious consideration to the content and quality of the testing material that you are using. This is only done by careful clinical observation comparing both commercial and fresh foods in your own practice.

Appendix B Selection, Sources, Preparation and Storage of Foods Commonly Used In Patch Testing

Food Selection

Milk, egg, peanut, wheat, soy bean, white potato, corn, rice, barley, oats, beef, chicken, turkey, ham, carrot, peas, green beans, peaches, and apples. Additional foods can be added based on history and diet.

Food Sources:

Food extracts supplied by commercial laboratories are not suitable for patch testing. All foods must be in a paste form in order to place them in the Finn chamber.

Grains and flours:

Bob's Red Mill (800-349-2173: bobsredmill.com) is an excellent source of grains. They have available numerous flours including wheat, barley, corn, rice, soy, oats and potato.

Byrd Mill (byrdmill.com) 2% Fat-Light Roast Peanut Flour

Barry Farm (barryfarm.com) whole milk powder, whole egg powder

Jarred baby foods are sources of beef, chicken, turkey, ham as well as vegetables and fruits.

The Food Preparation

1. Preparation of patch test material from powders

Powder can generally be made into a paste suitable for patch testing by mixing 2 g of the powder with 2 cc of sterile water. An easy technique is to use a triple beam balance or digital scale. Use a small plastic medicine cup for mixing. Fill the cup with approximately 2 g of powder, easily removed from a container with a tongue depressor and add 2 cc of water and then mix into a paste. Whole milk powder will require 3 g of powder for 1 cc of water. We have found that it is best when the food has the consistency of “cake frosting”.

2. Preparation of foods from baby foods

Stage 1 baby foods can be used for a number of foods used in patch testing. It should be noted that some of the baby foods particularly the fruits and vegetables contain too much water to allow easy placement in a Finn chamber. We recommend the following technique: Label a paper towel with the baby food that is being prepared. Place a generous amount of the food onto a small stack of labeled paper towels. Allow the excess liquid to absorb into the paper towels. When the food becomes the consistency of cake batter it is ready for use. This sometimes requires scooping the food and moving it to various areas on the paper towel to get the proper consistency.

Suggestions: We have found that wheat, white potato and corn harden quickly in the capped syringe. Therefore these foods are made at the time of patch testing and applied directly into the Finn chamber with a small stir straw. We do the same for these foods when used for prick testing.

Storage of Foods

Upon receiving 1 pound packages of each of the foods to be used for patch testing, individual Tupperware containers are filled with approximately 6 ounces of powder. These are labeled and stored in the freezer. Removing powder from a one-pound bag is too cumbersome for easy preparation.

Once the foods have been prepared to the consistency that is appropriate for patch testing we then transfer approximately 2 ml of the food into a 3 mL BD Oral Dispensing Syringe. These are available as unsterilized packages of 100 with a cap. Each syringe is filled using a stir straw or tongue depressor, labeled, capped and stored. Foods are changed each month.

Filling the Finn chamber:

Using the 3 cc syringe, place the tip on the base of the Finn chamber at a 45 degree angle. Slowly depress the plunger until the Finn chamber is fall. For wheat, corn and potato preparer the material at the time of patch testing and place a small "glob" into the Finn chamber using a stir straw. Practice filling Finn chambers before your first patch test.

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Stepwise Approach to Reintroduction of Foods in Patients with EoE Treated with Six-Food Elimination Diet (SFED)

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- If remission* achieved after eliminating six foods (cow's milk, wheat, egg, soy, peanuts/tree nuts and all seafood) then ***soy*** reintroduced in the diet. Upper endoscopy (EGD) repeated in 6 weeks.
- If histological remission on esophageal biopsies: soy is kept in the diet and ***egg*** reintroduced. However if histological relapse** then soy eliminated and egg reintroduced followed by repeat EGD with esophageal biopsies in 6 weeks.
- Histological remission on esophageal biopsies after egg then in addition to egg ***wheat*** added to the diet. However if relapse with egg then egg replaced with wheat and EGD with esophageal biopsies in 6 weeks.
- If histological remission after challenge with wheat then ***cow's milk*** added to diet. However if relapse after wheat then wheat replaced with cow's milk.
- Histological remission after cow's milk challenge is followed by reintroduction of ***peanut/tree nuts*** to the diet. In case of relapse cow's milk is replaced with peanut/tree nuts followed by EGD with esophageal biopsies in 6 weeks.
- If histological remission is maintained after introduction of peanut/tree nuts then ***seafood*** is added to the diet. In case of relapse peanut/tree nuts are replaced with seafood and EGD with esophageal biopsies repeated in 6 weeks.
- At the end of this reintroduction process patient has demonstrated relapse with one or more foods and this/these foods alone are excluded from the diet.
- One year later the patient is re-challenged with the excluded food(s) to assess if tolerance to the food has developed. If not, then the process is repeated yearly with the identified foods.

* Remission = esophageal eosinophil count $\leq$15/hpf
** Relapse = esophageal eosinophil count >15/hpf

Outcome of Various Dietary Approaches in Eosinophlic Esophagitis

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Author	No.	Allergy Tests	Diet	Outcome	Residual Eosinophil Count
Kelly et al.[1]	10	SPT 6/9	Elemental diet	Clinical impr. 10/10 **(100%)** Histologic improvement 9/10 **(90%)**	 0.5
Teitelbaum et al.[2]	11	SPT/ RAST	Allergy test based elimination	No improvement	Not available
Noel et al.[3]	10	SPT	Elimination diet	No response	Not available
Spergel et al.[4]	146	SPT & APT	Elimination diet	Significant impr. 112 **(77%)** Partial response 19 **(13%)** Treatment failure 15 **(10%)**	1.1 ± 2.1 12.0 ± 3.2 36.3 ± 14.9
Liacouras et al.[5]	172	SPT & APT	Elemental diet	Significant clinical & histologic improvement = 160/164 **(98%)**	1.1 ± 0.6
Kagalwalla et al.[6]	35	Allergy tests not utilized	Std 6-food elim diet	Significant impr. 26/35 **(74%)** Partial response 3/35 **(9%)**	3.1 ± 3.2 15.7± 2.1
Kagalwalla et al.[6]	25	Allergy tests not utilized	Elemental diet	Significant impr. 22/25 **(88%)** Partial response 2/25 **(8%)**	1.6 ± 2.1 15.0 ± 2.8
Gonsalves et al.[7]	18	SPT	Std 6-food elim diet	Significant clinical & histologic improvement = 14/18 **(78%)**	Not available

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